The Chemical Company

January 16, 2015

Via CDX

TSCA Confidential Business Information Center (7407M)
EPA East - Room 6428 Attn: Section 8(e)
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20004-3302

Subject: Notice in Accordance with TSCA Section 8(e): Results of a Local Lymph Node Assay (LLNA) n mice with 3-methyl-1-(2,6,6-trimethylcyclohex-1-en-1-yl)penta-1,4-dien-3-ol

Dear Section 8(e) Coordinator:

BASF Corporation is submitting the results of a skin sensitization study with 3-methyl-1-(2,6,6-trimethylcyclohex-1-en-1-yl)penta-1,4-dien-3-ol (CASRN 5208-93-5), conducted by Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany. The test substance is a precursor for vitamin and carotenoid production.

In this study the test item was assessed for its skin sensitizing potential using the Local Lymph Node Assay (LLNA) in mice. Test item solutions at different concentrations were prepared in the vehicle MEK.

The local lymph node assay is recommended by international test guidelines (e.g., OECD) as an animal test for predicting skin sensitization in humans and provides a rational basis for risk assessment. The basic principle underlying the LLNA is that sensitizers induce a primary proliferation of lymphocytes in the lymph node draining the application site. The ratio of proliferation in test item treated groups compared to that in vehicle controls is termed the Stimulation Index (S.I.). Radioactive labeling is used to measure cell proliferations.

For this purpose a local lymph node assay was performed using test item concentrations of 2, 5, and 10% (w/w). The highest concentration tested was the highest concentration that could be achieved whilst avoiding systemic toxicity and excessive local skin irritation (as determined by two pre-experiments).

The animals showed neither signs of systemic toxicity nor local skin effects during the course of the study and no cases of mortality were observed. A statistically significant or biologically relevant increase in ear weights was not observed in any treated group in comparison to the vehicle control group. Furthermore, for BALB/c mice, a cut-off value of 1.1 for the ear weight index was reported for a positive response regarding ear skin irritation. None of the indices determined for the test item treated groups reached or exceeded this threshold.

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A test item is regarded as a sensitizer in the LLNA if exposure to one or more test item concentration results in a 3-fold or greater increase in incorporation of ^{3}HTdR compared with concurrent controls, as indicated by the Stimulation Index (S.I.). The estimated test item concentration required to produce a S.I. of 3 is referred to as the EC3 value.

In this study Stimulation Indices (S.I.) of 3.83, 8.10, and 8.28 were determined with the test item at concentrations of 2, 5, and 10% (w/w) in MEK, respectively. A dose response was observed.

An outlier was identified in the vehicle control group (DPM value determined for animal number 4). However, as exclusion of the outlier did not change the overall test result, the value in question was not excluded from any calculation.

A statistically significant and biologically relevant increase in DPM value was observed in all dose groups in comparison to the vehicle control group. Additionally, a statistically significant and biologically relevant increase in lymph node weights and -cell counts was observed in all treated groups in comparison to the vehicle control group. Furthermore, the cut-off value of 1.55 for a positive response regarding the lymph node cell count index reported for BALB/c mice was exceeded in all dose groups (indices of 1.92, 2.48, and 2.61, respectively).

Thus, the test item **3-methyl-1-(2,6,6-trimethylcyclohex-1-en-1-yl)penta-1,4-dien-3-ol was found to be a skin sensitizer**. An EC3 value could not be derived, since all S.I.s were above the threshold index of 3.

BASF Corporation understands that reporting of the results from this study under TSCA 8(e) is in accordance with EPA's policy.

Please note the technical contact and address below and direct all correspondence regarding this submission accordingly. If you have any questions, please call (248) 948-2051.

Sincerely,

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